the specification so as to enable one skilled in the art to practice the invention.

Applicants respectfully traverse this ground of rejection since it is believed that the claims are based upon an enabling disclosure. The claims objected to by the Examiner are directed to a method for blocking somatostatin receptors in warm blooded animals and to treat the diseases associated therewith as clearly set forth in the specification. The Examiner's attention is directed to the discussion of the prior art as set forth on pages 1 and 2 of the specification and it is clearly stated on page 3 that the object is to treat the pathological states or diseases in which somatostatin receptors are involved. In addition, on page 40, there is a study of the bond to somatostatin receptors which clearly demonstrates that the specification is enabling for a method for blocking somatostatin receptors. Therefore, the specification is enabling and withdrawal of this ground of rejection is requested.

All of the claims were rejected under 35 USC 112, second paragraph, as being indefinite for the reasons set forth on pages 4 to 9 of the specification.

Applicants respectfully traverse these grounds of rejection since it is believed that the amended claims are in compliance with 35 USC 112.

With respect to claims 3, 4, 9 and 10, it should be noted that it is deemed that the claims do set forth steps for use of the invention. The claim clearly calls for administering to warm-blooded animals an effective amount of the active ingredient and this is clearly a step which is well known and recognized by the Patent Office as can be seen from millions of claims drawn in this fashion. Moreover, Applicants have shown by the test data on page 40 that the compounds are active for the desired results.

With respect to the objections set forth in paragraph E, the typographical error in claim 10 has been corrected and the oxygen and sulfur have been rewritten as suggested by the Examiner. The period in claim 10 has been changed to a comma and "or" has been deleted. In addition "said pathological disorders" has been changed to "block somatostatin receptors" which is in accordance with the beginning of the claim. Claim 11 has been corrected to recite the substituent in R' and the definition of X' has been corrected. Claim 5 has been cancelled to obviate the rejections thereto. Claim 3 has been amended to correct tertiary butyl. Therefore, the amended claims are believed to comply with 35 USC 112, second paragraph, and withdrawal of these grounds of rejection is requested.

Claims 5 and 11 were rejected under 35 USC 102 as being anticipated by the Prunonosa et al reference or the Girault et al reference and by the Weber et al reference as well the Braquet et

al reference and the Miyazawa et al reference. Claim 11 was further rejected as being anticipated by the Okano et al reference. All of the claims were rejected under 35 USC 103 as being obvious over the Tahara et al reference.

Applicants respectfully traverse these grounds of rejection since the references do not anticipate or render obvious the claims in view of the amendments thereto. With respect to the Prunonosa et al reference, this is excluded by the disclaimer i) by the addition of 4-hydroxy-phenyl in the definition of R'. With respect to the Girault et al reference, this is excluded by the ii) disclaimer of 4-hydroxy-phenyl in the definition of R'. With respect to the Weber et al reference, this is excluded by the disclaimer iiiiiii) wherein X' is a covalent bond and Y' is oxygen. In the definition of X' in the iiii) disclaimer, a covalent bond has been deleted. With respect to the Braquet et al reference, this is excluded by the disclaimer in i). With respect to the compounds wherein R_1', R_{2a}', R_{2b}', R_3' and W' are respectively O-Cl; H; H; methyl and (2-chloro-phenyl)-NH-CS- is not described in the Braquet et al reference. The compound wherein the said substituents are respectively O-Cl; H; H; methyl and (2,3-dichloro-phenyl)-NH-CO- is the closest compound in this reference and this is excluded by the disclaimer i).

With respect to the Miyazawa et al reference, the closest compound therein is excluded by the disclaimer iiiiiii). The

compound wherein R'_1, R_{2a}', R_{2b}', R'_3 and W' respectively are oCl; H; H; methyl and (4-fluoro-phenyl)-CH_2-CO- falls within the disclaimer of iiiii). With respect to the Okano et al reference, the closest compounds are excluded by the disclaimer iiiii). Therefore, none of the references cited by the Examiner anticipates the present claims.

With respect to the obviousness type rejection based on the Tahara et al reference, this discloses the use of some diazapines for the treatment of osteoporosis and the measured activity is the bone resorption-inhibitory effect. This in no way suggests an affinity of the said diazapines on somatostatin receptors as claimed by Applicants and therefore, there is no suggestion of using diazapines to treat illnesses in which somatostatin receptors are involved and this is an entirely different reaction. Therefore, the same does not render obvious Applicants' claimed method and withdrawal of this ground of rejection is requested.

In view of the amendments to the claims and the above remarks, it is believed that the claims clearly point out Applicants' patentable contribution and favorable reconsideration of the application is requested.

Respectfully submitted,
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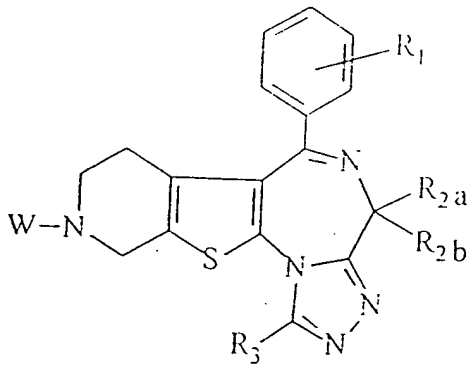
CAM:ds
Enclosures

MARKED UP VERSION OF CLAIMS SHOWING CHANGES MADE

Claim 9 (amended) A composition for blocking somatostatin receptors comprising an amount of a compound [of] as defined in claim 10 sufficient to block somatostatin receptors and an inert pharmaceutical carrier.

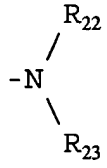
Claim 10 (amended) A method for blocking somatostatin receptors in warm-blooded animals in need thereof comprising administering to warm-blooded animals an effective amount of a compound selected from the group consisting of a compound of the formula



I

wherein W is hydrogen or R-X-C(Y)-, R is unsubstituted or substituted aryl or heteroaryl with at least one substituent selected from the group consisting of lower alkyl, lower alkoxy, lower alkylthio, lower alkoxycarbonyl, lower alkylsulfonyl, halogen, $-CF_3$, $-OCF_3$, -OH, $-NO_2$, -CN, aryl, aryloxy, [cycloalkly] cycloalkyl and heterocycloalkyl, X is $-(CH_2)_n-Z$, Z is selected from

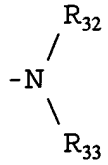
the group consisting of a covalent bond, -NH-, [=O] -O- and [=S] -S-, n is 0, 1 or 2, Y is oxygen or sulfur, R_1 is selected from the group consisting of hydrogen, -OH, halogen, lower alkyl and lower alkoxy, the alkyl and alkoxy being unsubstituted or substituted with at least one member of the group consisting of $-CF_3$, lower alkoxy, $-NH_2$ and mono- and di-lower alkylamino[.], R_{2a} and R_{2b} are individually selected from the group consisting of hydrogen, substituted or unsubstituted lower alkyl, substituted or unsubstituted lower alkenyl, substituted or unsubstituted lower alkynyl and $-Z_{21}-R_{21}$, the substituents being at least one member of the group consisting of halogen,



, $[R_{21}-Z_{21}]$ and $Z_{22}-R_{24}$,

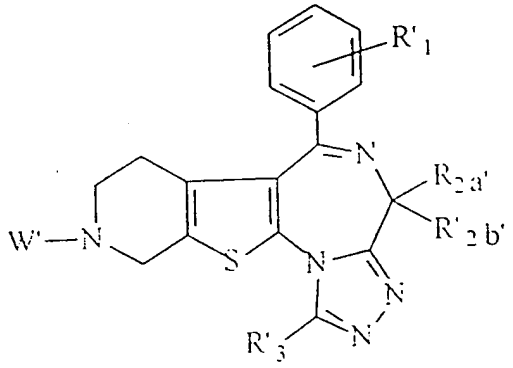
R_{22} and R_{23} are individually selected from the group consisting of hydrogen, lower alkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heteroaryl, [or] heteroarylalkyl, alkylsulfonyl, cycloalkylsulfonyl, arylsulfonyl, lower alkoxycarbonyl, aryloxycarbonyl, alkylcarbonyl, arylcarbonyl and cycloalkylcarbonyl, Z_{21} and Z_{22} are individually selected from the group consisting of oxygen, sulfur, -CO- and -O-CO-, R_{24} is selected from the group consisting of hydrogen, lower alkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heteroaryl, heteroarylalkyl, alkylsulfonyl, cycloalkylsulfonyl and arylsulfonyl, R_{21} is selected from the group consisting of hydrogen, lower alkyl, aryl and aralkyl, R_3 is selected from the group consisting of hydrogen,

halogen, $-NO_2$, -CN, unsubstituted or substituted alkyl of 1 to 10 carbon atoms, unsubstituted or substituted lower [alkyl] <u>alkenyl</u>, unsubstituted or substituted lower alkynyl, unsubstituted or substituted cycloalkyl, unsubstituted or substituted cycloalkylalkyl, unsubstituted or substituted aryl, unsubstituted or substituted aralkyl, unsubstituted or substituted lower aryloxalkyl, unsubstituted or substituted heteroaryl, unsubstituted or substituted heteroarylalkyl and $-Z_{31}R_{31}$, the substituents being selected from the group consisting of halogen, aryl,



and $-Z_{32}-R_{34}$, $-Z_{31}$ is selected from the group consisting of -O-, -C(O)-, -OC(O)- and -S-, R_{31} is selected from the group consisting of hydrogen, lower alkyl, aryl and lower aralkyl, R_{32} and R_{33} are individually selected from the group consisting of hydrogen, lower alkyl, aralkyl and alkylcarbonyl or together with the nitrogen form a heterocyloalkyl, Z_{32} is selected from the group consisting of oxygen, sulfur, -C(O)-, -S(O), [-OCO-] <u>-O-CO-</u> and $-SO_2$, R_{34} is selected from the group consisting of hydrogen, lower alkyl, aryl and lower aralkyl and its non-toxic, pharmaceutically acceptable salts sufficient to [treat said pathological disorders] <u>treat somatostatin receptors</u>.

Claim 11 (amended) A compound of the formula



II

wherein W′ is hydrogen or -C(Y′)-X′-R′, R′ is selected from the group consisting of phenyl, naphthyl, indolyl and pyridyl, all unsubstituted or substituted with at least one member of the group consisting of methyl, ethyl, propyl, isopropyl, butyl, tert.-butyl, methoxy, ethoxy, methylthio, ethylthio, methoxycarbonyl, ethoxycarbonyl, methylsulfonyl, ethylsulfonyl, chlorine, fluorine, bromine, trifluoromethyl, trifluoromethoxy, -OH, $-NO_2$, -CN, phenyl, phenoxy and morpholino, X′ is selected from the group consisting of $-CH_2-$, $-CH_2-CH_2-$, $-CH_2NH-$, -NH-, -O-, -S- and a covalent bond, Y′ is oxygen or sulfur, R'_1 is at least one member of the group consisting of hydrogen, chlorine, methyl and methoxy, R'_{2a} and R'_{2b} are individually hydrogen or methyl, R'_3 is selected from the group consisting of hydrogen, methyl, ethyl, propyl, butyl, pentyl, hexyl, heptyl, methoxyethyl, ethoxyethyl, dimethylaminoethyl, cyclohexylmethyl, phenyl, diphenyl, benzyl unsubstituted or substituted with -OH or methoxy, phenethyl, naphthylmethyl and indolylmethyl excluding the compounds of Formula II wherein a) W′ is hydrogen, R'_1 is o-chlorine, R'_{2a} is hydrogen, R'_{2b} is hydrogen or methyl and R'_3 is methyl and b) wherein W′ is -[(Y)C-X′-R′] C(Y′)-X′-R′ and i) X′ is -NH-, Y′ is oxygen, R'_1 is o-chlorine, R'_{2a} and

R'_{2b} are hydrogen, R'_3 is methyl and R' is selected from the group consisting of 4-tert.butyl-phenyl, 4-trifluoromethyl-phenyl, 4-hydroxyl-phenyl, 4-methoxy-phenyl, 3,4,5-trimethoxy-phenyl, 2,3-dichloro-phenyl, 2,[3]4-difluoro-phenyl, 4-phenoxy-phenyl, pyridinyl and cyanophenyl or ii) X' is -NH-, Y' is sulfur, R'_1 is o-chloro, R'_{2a} and R'_{2b} are hydrogen, R'_3 is methyl and R' is selected from the group consisting of 4-hydroxy-phenyl, 4-tert.butyl-phenyl, 2,4-ditert.butyl-phenyl, 2-trifluoromethyl-phenyl, 3-trifluoromethyl-phenyl, 4-trifluoromethyl-phenyl, 4-methoxy-phenyl, 3,4,5-trimethoxy-phenyl, 4-fluoro-phenyl and 4-methylsulfonyl-phenyl or iii) X' is $-CH_2-NH-$, Y is oxygen, R'_1 is o-chlorine, R'_{2a} and R'_{2b} are hydrogen, R'_3 is methyl and R' is phenyl, or iiii) X' is oxygen [or a covalent bond], Y' is oxygen, R'_1 is o-chlorine, R'_{2a} and R'_{2b} are hydrogen, R'_3 is methyl and R' is pyridyl or cyanophenyl or iiiii) X' is [hydrogen] CH_2, Y' is oxygen, R'_1 is O-chlorine and R'_{2a} and [R_{2a}'] R'_{2b} are hydrogen, R'_3 is methyl and R' is phenyl or 4-fluoro-phenyl or iiiiii) X' is $-CH_2-CH_2-$, Y' is oxygen, R'_2 is o-chloro, [R_{2a}'] R'_{2a} and R[$_{2b}$'] R'_b are hydrogen, R'_3 is methyl and R' is phenyl or iiiiiii) X' is a covalent bond and Y' is oxygen.

Claim 3 (twice amended) The method of claim 10 wherein W [represents the] is selected from the group consisting of hydrogen [atom] or [a radical of formula] R-X-C(Y)-;
R [represents] is selected from the group consisting of phenyl, naphthyl, indolyl and [or] pyridyl, [radical, these radicals being optionally] all unsubstituted or substituted by at least one member

[or more identical or different substituents chosen from the following radicals:] is selected from the group consisting of methyl, ethyl, propyl, isopropyl, butyl, tert-butyl, methoxy, ethoxy, methylthio,ethylthio, methoxycarbonyl, ethoxycarbonyl, methylsufonyl [methylsuphonyl], ethylsulfonyl [ethylsuphonyl], chloro, fluoro, bromo, trifluoromethyl, trifluoromethoxy [trifluoromethyloxy], hydroxy, nitro, cyano, phenyl, phenoxy and [or] morpholino;

X [represents] is selected from the group consisting of CH_2, C_2H_4, CH_2NH, NH, O, S or a covalent bond;

Y [represents] is selected from the group consisting of O or S;

R_1 [represents] is selected from the group consisting of one of [or more identical or different groups, chosen from:] hydrogen atom, a chloro, methyl or methoxy radical;

R_{2a} and R_{2b} [represent, independently the] are selected from the group consisting of a hydrogen atom or a methyl [radical];

R_3 [represents the] is selected from the group consisting of a hydrogen atom, methyl, ethyl, propyl, butyl, pentyl, hexyl, heptyl, methoxyethyl, ethoxyethyl, dimethylaminoethyl, cyclohexylmethyl, phenyl, diphenyl, benzyl [optionally substituted] unsubstituted or substituted by the hydroxy or methoxy, phenethyl, naphthylmethyl or indolylmethyl [radical].